

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

SHIMADA et al.

Application No. 09/486,823

Filed: March 3, 2000

For: THERAPEUTIC AGENT FOR

NEURODEGENERATIVE DISORDERS



Examiner: SPIVACK, P

Group Art Unit: 1614

DECLARATION UNDER 37 C.F.R. §1.132

Honorable Commissioner of
Patent and Trademarks
Washington, D.C. 20231

Sir:

I, Shinichiro Toki, a citizen of Japan, do hereby declare
as follows:

I graduated from Kyoto University, Faculty of Agriculture
in 1985, entered the graduate school of Kyoto University
immediately after graduation, and got MSc degree in 1987. My
major subject in Kyoto University was applied to microbiology.
From 1987 to 1999, I had worked at Tokyo Research Laboratories,
Kyowa Hakko Kogyo Co., Ltd. At Tokyo Research Laboratories, I
studied on secondary metabolites of microorganisms and
pharmacological effects of the metabolites on
physiologically-important proteins and on animal and/or human
cells. I got Ph.D. degree from Kyoto University, Faculty of
Agriculture in 1995. During 1997 and 1998, I stayed in Department
of Brain and Cognitive Sciences, Massachusetts Institute of
Technology, U.S.A. and studied on the distribution and
physiological function of novel guanine nucleotide exchange
factors in rat brain in the lab. In 1999, I moved to Pharmaceutical
Research Institute, Kyowa Hakko Kogyo Co., Ltd., and since then,
I have been studying on pharmacological effects of various
compounds on physiologically-important proteins, animal and/or
human neuronal cells, and animal models of various neural diseases.

Since 2000, I have been a senior researcher and been at the position of the head, Department of Neurobiology, Drug Discovery Research Laboratories, Pharmaceutical Research Institute, Kyowa Hakko Kogyo Co., Ltd. I belong to the Japanese Biochemical Society, Japan Society of Bioscience, Biotechnology, and Agrochemistry, the Japanese Society for Neurochemistry, and the Society for Neuroscience. The number of my oral and poster presentations in the academic meetings of these and other international societies, such as the International Conference on Amino Acid Research, the International Society of Cerebral Blood Flow and Metabolism is more than fifteen in total. The number of my publications in academic journals is more than twenty; these journals include Journal of Biological Chemistry, Journal of Antibiotics, Molecular Pharmacology, European Journal of Pharmacology, etc.

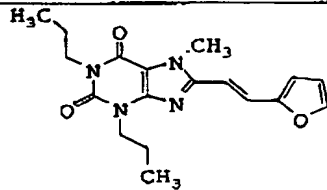
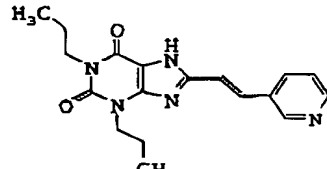
The following experiment was conducted under my direction.

EXPERIMENT

Test Compounds:

The following compounds:

Table 1

Compound No.		
A	1,3-Dipropyl-8-[2-(E)-(2-furyl)vinyl]-7-methylxanthine	
B	1,3-Dipropyl-8-[2-(E)-(3-pyridyl)vinyl]-xanthine	

Method:

The same method as in Test Example 1 (page 9, line 16 to page 11, line 16) of the present application was employed except that the administration amount of the test compound was 100 mg/kg

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(p.o.).

Result:

Table 2

Test groups	
Control	615.9±39.6
MPTP HCl	279.1±26.8 ###
MPTP HCl + Compound A	330.4±22.2
MPTP HCl + Compound B	434.5±24.3 **

• **: $p < 0.01$ (compared with the group given MPTP HCl alone).

###: $p < 0.001$ (compared with the control group).

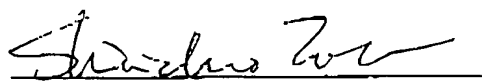
(n = 9 to 10; Wilcoxon rank sum test)

Conclusion:

As apparent from Table 2, Compound A and Compound B exhibited neurodegeneration inhibiting activity.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: Mar. 5 2001


Shinichiro Toki